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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/335,686	06/18/1999	RANDOLPH J. NOELLE	012712-696	6750

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PILLSBURY WINTHROP, LLP
P.O. BOX 10500
MCLEAN, VA 22102

EXAMINER	
GAMBEL, PHILLIP	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 12/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/335,686	NOELLE, RANDOLPH J.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44-46 and 49-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44-46 and 49-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114.
Applicant's submission filed on 11/12/03 has been entered.

Claims 44-46 and 49-55 are pending and being acted upon presently

Claims 1-43 and 47/48 have been canceled previously.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.

Given the absence of additional rebuttal to the outstanding rejections of record in applicant's request for a RCE, filed 11/12/03; the rejections are maintained for the reasons of record

3. Claims 44-46, 49 and 51-53 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Cobbold et al. (U.S. Patent No. 6,056,956) in view of Lederman et al. (U.S. Patent No. 5,474,771; 1449, #AA) OR Armitage et al. (U.S. Patent No. 6,087,329) for the reasons of record set forth in the previous Office Actions.

Claims 50, 54, 55 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Cobbold et al. (U.S. Patent No. 6,056,956) in view of Lederman et al. (U.S. Patent No. 5,474,771; 1449, #AA) OR Armitage et al. (U.S. Patent No. 6,087,329).
as applied to claims 44- 46, 9, 51-53 above
and in further view of Ramanathan et al. (WO 91/09059) for the reasons of record set forth in the previous Office Actions.

4. Applicant's arguments, filed 10/25/02 and 4/14/03, have been fully considered but are not found convincing essentially for the reasons of record.

Applicant's arguments and the examiner's rebuttal are essentially the same as of record.

Applicant argued that there was no reasonable expectation of success to achieve the claimed limitations of prolonged humoral suppression.

As previously argued, applicant asserted that the prior art references teach only that a gp39-specific antibody would have a transient, global effect on antibody production by B cells and are silent on the prolonged effect on a gp39 antagonist on T cells.

Applicant argued in conjunction with Schonrich et al. (Intl. Immunol. 4: 581-590, 1992) and Schneider et al. (Thymus 20: 5-15, 1992) disclose the induction of tolerance as of 1992 was unpredictable. Therefore, applicant asserts that the CD4-induced tolerance would not be sufficient to suggest that an anti-CD40L antibody would induce tolerance, especially as the induction of tolerance and the mechanisms associated therewith were poorly understood at the time of the invention.

With respect to tolerance, the following is noted.

Tolerance is the long-lasting nonreactivity of the immune system to a specific set for antigens, maintained without on-going immunosuppression. For example, many different strategies have been developed to achieve transplantation tolerance some have which led to indefinite graft survival in rodents, none of these strategies have yet been applied to human patients in a way that allows reliable withdrawal or exogenous immunosuppression. Auchincloss (chapter 11 in Transplantation Immunology, Bach and Auchincloss Eds. Wiley-Liss, New York, 1995, pages 211-218, see page 211). While tolerance inducing strategies that have worked well in rodents, such strategies have been much less successful even when tested in nonhuman primates and other large animals. Also, the Conclusion on page 217 states that Although more than a dozen different techniques to induce tolerance in rodents are now available, the fact remains that none of them has been used successfully in the clinic. Inducing transplantation tolerance in human must therefore be very hard to do. And that reading of this chapter should be wary of simple solution to this complex approaches Similarly, differences between antigens as well as species would be expected.

Further, the claims do not recite tolerance.

As indicated previously and in contrast to applicant assertions, the following of record is set forth to support the motivation and expectation of success at the time the invention was made to achieve the claimed limitations.

Cobbold et al. teach the use of CD4-specific antibodies to induce specific non-responsiveness or tolerance to various molecules, including globular proteins, glycoproteins and polypeptides intended for therapeutic use and allergens (see entire document; including column 2, paragraph 4; column 3, paragraphs 5-6).

Cobbold et al. teach the combined preparation for simultaneous, separate or sequential administration of antibody treatment to induce tolerance to an antigen (see column 2, paragraph 3), including a number of antigens (see column 2, paragraph 4). Cobbold et al. further teach that the antigen can be given at the time the course the immunosuppressive antibody treatment is commenced, that is, tolerance to an antigen can be induced under the cover to administering immunosuppressive antibodies (see column 3, paragraphs 5-6).

Cobbold et al. differ from the claimed methods by not teaching the preferred embodiments of targeting the CD40L/gp39 expressed on T cells with CD40L-specific antibodies.

Lederman et al. teach inhibiting various immune responses with 5C8-specific antibodies (see entire document, including columns 6-7, 11); including allergies (column 11, paragraph 6). The 5C8 specificity is the equivalent of human CD40L. Ldederman et al. Teach effective inhibiting amounts, including amounts to inhibit T cell activation of B cells (see columns 10-11, overlapping paragraph). In addition, Lederman et al. also teach inhibiting immune responses such as transplant rejection and autoimmunity, responses associated with T cells (see column 11, paragraphs 4-5).

Armitage et al. teach inhibiting various immune responses with CD40 antagonists, including soluble CD40, CD40Ig, monomeric CD40L (e.g. columns 10-11, including overlapping paragraph, columns 14-17; column 21); including targeting allergies, including IL-4 induced IgE responses (e.g. column 10, paragraph 3 - column 11, paragraph 1; column 15, paragraph 1-2; Examples 8-11, 13).

In contrast to applicant's assertions of no connection between targeting CD4 and CD40L/gp39; the prior art of Cobbold et al., Lederman et al. and Armitage et al. all target the same cell, that is, the CD4 T helper cell with the motivation and expectation of success of inhibiting immune response to a broad variety of antigens, given the essential role of T helper cells in immune responses and regulation.

Also, in contrast to applicant's assertions, the prior art does teach achieving specific non-responsiveness or specific unresponsiveness to antigens of interest, including those thymus-dependent antigens encompassed by the claimed methods.

Given such specific unresponsiveness, the long term specific unresponsiveness would have been expected to be maintained for a prolonged period of time, including after clearance of CD40L-specific antibodies. This is not to say that additional treatment could be forthcoming but the ordinary artisan would have expected that prolonged suppression would have been achieved by achieving the endpoint of specific nonresponsiveness at the time the invention was made.

Given the ability of 5C8-/CD40L-specific antibodies, as taught by Lederman et al. OR the ability of various CD40 antagonists, as taught by Armitage et al. to inhibit various immune responses, including T helper cell-mediated immune responses, including humoral responses, including their use in therapeutic modalities of treating autoimmune and allergic responses; one of ordinary skill in the art at the time the invention was made would have been motivated to substitute these antagonists into the methods of Cobbold et al. to similarly target T helper cells to inhibit humoral responses to thymus-dependent antigens. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Also, as pointed out previously, the following is noted.

Ramanathan et al. teach the use of IL-4-specific antagonists such as IL-4-specific antibodies to inhibit or treat allergic responses (see entire document, including page 1, paragraph 3; Summary of the Invention; Description f the Invention, page 6, paragraph 2, pages 13-16).

Combination therapy was known and practiced at the time the invention was made.
It was prima facie obvious to combine two compositions each of which is taught by prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose; idea of combining them flows logically from their having been individually taught in prior art. In re Kerkhoven, 205 USPQ 1069, CCPA 1980. See MPEP 2144.

Given the prior art teachings of using both CD40:CD40L-specific inhibitors and IL-4-specific inhibitors to inhibit allergic responses; the ordinary artisan would have been motivated to combine both said inhibitors to down regulate responses to allergens at the time the invention was made.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments have not been found persuasive.

5. Claims 44-46 and 49-55 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-17 of U.S. Patent No. 5,942,229 for the reasons of record.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the patented claims anticipate the instant method claims.
In addition, when the instant claims are read in light of the specification; the patented claims are the preferred embodiments and again anticipate the instant claims.

Applicant's amendments, filed 9/24/01 and 4/14/03, requested that this rejection be stayed in abeyance until the subject application is otherwise in condition for allowance.

6 No claim is allowed.

7. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

After January 20, 2004, Phillip Gambel's telephone number will be (571) 272-0844 and Christina Chan's telephone Number will be (571) 272-0841.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 872-9306.

Phillip Gambel, Ph.D.
Primary Examiner
Technology Center 1600
December 1, 2003

John J. Doll, Director
Technology Center 1600